Intracranial Metastasis from Clear Cell Sarcoma of the Kidney
- A Case Report -

Childhood kidney tumors seldom metastasize into the cranial cavity unless it is a special histological variant. We report a 4-year-old boy with multiple intracranial metastases in the left parietotemporal and right cerebellar area from primary clear cell sarcoma of the kidney without evidence of bony metastases. Metastatic tumor revealed nests of uniformly polygonal cells with clear cytoplasm demarcated by delicate fibrovascular arcades. Tumor cells were positive for vimentin and negative for cytokeratin, S-100 protein, desmin, and myoglobin. Cellular proliferation rate measured by PCNA, and Ki-67 was not significantly different between primary tumor mass and metastatic brain lesion. Expression of p53 oncoprotein was not evident in both lesions. These findings suggested that the relapse and metastasis of clear cell sarcoma of the kidney was probably due to regrowth of micrometastases which were present at an early stage of disease.
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Key Words : *Sarcoma, Clear cell; Kidney neoplasms; Neoplasm metastasis*

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INTRODUCTION

Clear cell sarcoma of the kidney (CCSK), also known as bone-metastasizing renal tumor, is an uncommon but distinctive renal tumor of children with a characteristic histologic pattern and a marked proclivity for bone metastases (1). The most common site of metastasis is the skeleton, particularly the skull. Metastases also occur in regional lymph node, lung, liver, and rarely the brain. As a rule bone metastases precede the development of distant metastases elsewhere (2). We recently experienced an unusual case of CCSK which metastasized to brain without evidence of bony metastases. We report the histologic findings, cellular proliferation rate measured by immunostaining of PCNA, Ki-67, and expression of p53 oncoprotein of both primary and metastatic lesions of CCSK.

CASE REPORT

A 2 year-old-boy was admitted to the Department of Pediatrics, Seoul National University Children's Hospital with a right-sided abdominal mass in February 1994. Computed tomography of the abdomen revealed a huge tumor mass arising from the right kidney. A needle biopsy of renal mass was performed and a diagnosis of Wilms' tumor of blastemal type was made. Metastases to other organs was not evident on bone scan and other studies. Preoperative chemotherapy (vincristine, actinomycin, adriamycin, cyclophosphamide, and VP-16) followed by a right radical nephrectomy was performed. A

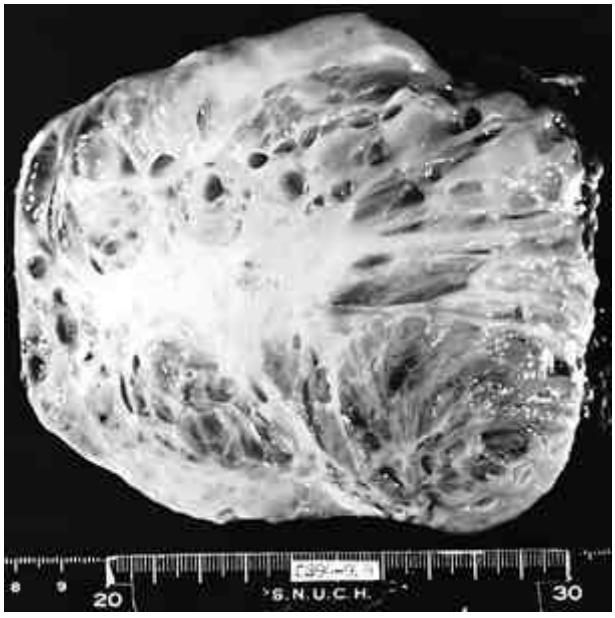

Fig. 1. Cut section of the right kidney shows a relatively well circumscribed tumor mass with multiple cystic spaces and solid areas with central stellate fibrous portion.

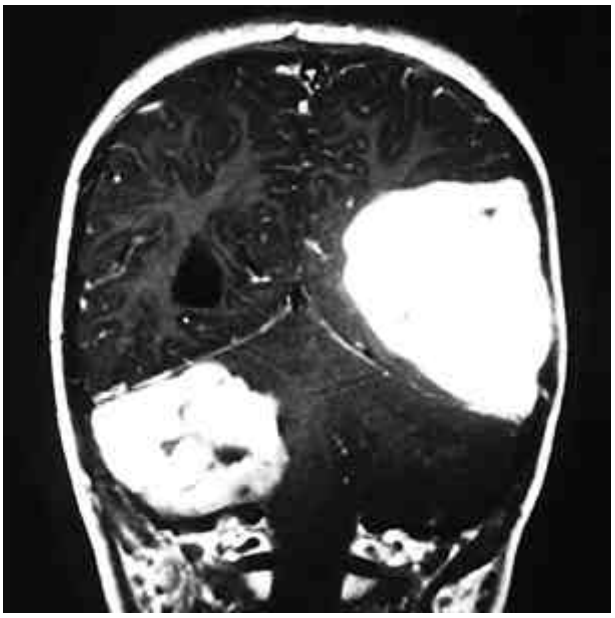

Fig. 2. A post-contrast T1 weighted coronal MR image reveals two well-enhancing extraaxial tumor masses on the left parietotemporal area and right cerebellum.

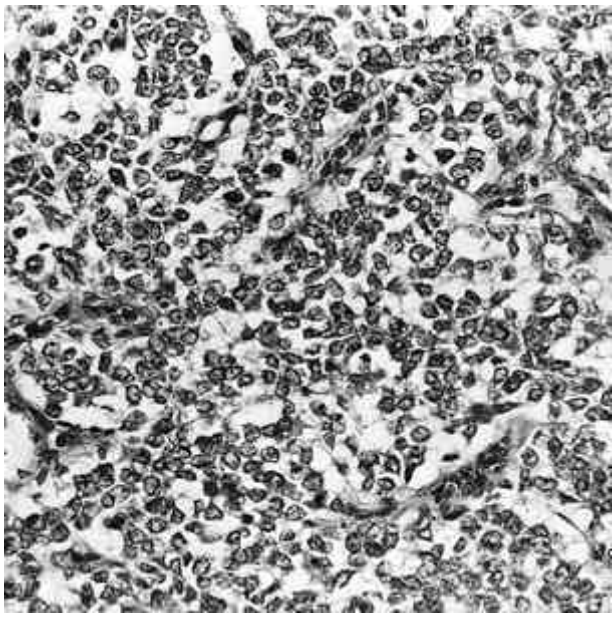

Fig. 3. Photomicrograph of the tumor mass shows nests of uniformly polygonal cells with clear cytoplasm demarcated by fibrovascular network (H&E, ×200).

large well circumscribed tumor mass bulging out within the renal capsule, 13.5×12.5 cm in size, was noted. The residual renal parenchyma was compressed peripherally. A cut section of the mass showed multiple cystic spaces filled with yellowish fluid, and also contained solid areas with central stellate scar (Fig. 1). Histopathologic diagnosis was further defined as clear cell sarcoma of the kidney confined to the renal capsule. Thereafter postoperative chemotherapy and radiotherapy (1080 cGY) were performed and completed by June 1995.

On November 1996 the patient developed headache, vomiting, and gait disturbance. An MR imaging of the brain revealed two huge, extraaxial tumor masses in the left parietotemporal area and right cerebellum, measuring 5 cm and 6 cm in diameter, respectively (Fig. 2). The patient was admitted for open brain biopsy of the left parietotemporal area mass. An open biopsy revealed a hypovascular, pink rubbery mass attached to the overlying dura mater. Frozen section was compatible with metastatic clear cell sarcoma of the kidney. The patient underwent postoperative chemotherapy. Bone scan and other studies revealed no metastatic foci except for the brain.

Histologic findings of the right kidney mass and metastatic brain lesion were similar. They revealed diffuse proliferation of nests of polygonal cell with clear cytoplasm demarcated by a fibrovascular network (Fig. 3). The tumor cell had an uniformly oval to round nucleus with fine, evenly granular cytoplasm. Sections from the renal mass revealed intravascular tumor emboli. Immunohistochemically, tumor cells were positive for vimentin, but negative for cytokeratin, S-100 protein, desmin, and myoglobin (Fig. 4). Cellular proliferation rate measured by PCNA (PC-10, DAKO), Ki-67 (MIB-1, Zymed) (percent of positive tumor cells) was not significantly different between primary renal tumor mass (PCNA; 17.5%, Ki-67; 18.2%) and metastatic brain lesion (PCNA; 19.3

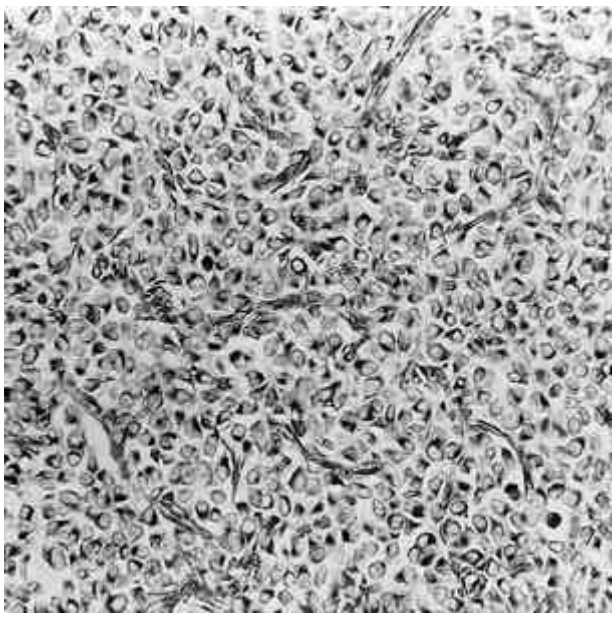

Fig. 4. Tumor cells show positivity for vimentin (Immunostain for vimentin, ×200).

%, Ki-67; 17.2%). Both lesions were negative for p53 oncoprotein (DO-7, DAKO).

DISCUSSION

Clear cell sarcoma of the kidney (CCSK) is a rare and highly malignant tumor comprising 4-6% of primary childhood renal tumors (3). As a clinicopathologic entity, CCSK was first recognized by Kidd in 1970 (4). Since then, additional cases have been added in the literature under the names of bone metastasizing renal tumor of childhood (1), undifferentiated sarcoma of the kidney (5) or sarcomatoid renal tumor of childhood (6). The origin of tumor cells of CCSK is unclear. Based on the combined histological, immunohistochemical, and electron microscopic features of CCSK, primitive mesenchymal cells which committed early stromagenic cells are strongly suggested as the origin tumor (7, 8).

Beckwith and Palmer (9) and Morgan et al. (5) classified CCSK as a variant of Wilms' tumor with different clinicopathologic behavior. However, there are many reasons that CCSK should be a separate entity. The recognition of CCSK is of practical importance because of its aggressive clinical behavior and poor prognosis necessitating aggressive therapy. There is a considerable difficulty in differentiating this tumor from the more commonly occurring Wilms' tumor on the basis of pathological findings. Compared to Wilms' tumor, CCSK reveals a poorly demarcated tumor margin, firmer consistency and frequent peripheral cystic change. Histologically, large vesicular nuclei with clear cytoplasm and characteristic arborizing fibrovascular network can help to establish the diagnosis of CCSK. However, in some cases, the diagnosis may be difficult especially in case of blastemal predominant Wilms' tumor in which blastemal cells show clear cell change. We presume that some of the reports of brain metastasis from Wilms' tumor prior to the recognition of CCSK as distinct entities were in fact CCSK. Immunohistologic studies are also useful for differential diagnosis. In Wilms' tumor, characteristic blastemal tissue is positive for cytokeratin and negative for vimentin. In contrast to Wilms' tumor, clear cells of CCSK are positive for vimentin and negative for cytokeratin (10). Flow cytometric analysis of CCSK revealed diploidy and different from those of Wilms' tumor with unfavorable histology showing aneuploid DNA pattern (11).

One of the most distinctive features of CCSK is its propensity for widespread metastases. As a rule bone metastases precede the development of distant metastases elsewhere (2). Although still quite rare, the greater incidence of brain metastasis in the more recent reports is probably due to improved detection and longer survival, and as the treatment and survival continue to improve, the incidences can be expected to increase (12).

In contrast to Wilms' tumor, the late onset of first relapse among cases of CCSK is a distinctive feature. The high relapse rates in patients with stage I tumors who were treated with protocols that did not include adriamycin suggest that these late metastases actually represent retarded or inhibited growth of micrometastases that occurred early in the course of the disesae (13). In our case, the cellular proliferation rate of the primary renal tumor and the metastatic brain lesion was not significantly different, and mutant oncoprotein expression, i.e., p53 oncoprotein, was not evident. Kumar et al. (14) showed that CCSK had nearly diploid DNA pattern and poor prognosis at least in this tumor type could not be explained on the basis of DNA content. Furthermore, the primary renal mass revealed evidence of microscopic intravascular tumor emboli. It may be that angiogenic potential or inappropriate chemotherapy of this tumor type is responsible for its aggressive behavior. All these findings support the theory that relapse and metastasis of primary CCSK is not due to the increase of aggressiveness, but to the regrowth of micrometastases which are present at an early stage of the disease.

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